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Letter to the Editor

Rapid Publication

11Q DUPLICATION IN A PATIENT WITH PITT-ROGERS-DANKS PHENOTYPE.

To the Editor:

In 1984 Pitt et al. described 4 patients with severe pre- and postnatal growth retardation, microcephaly, an unusual and characteristic facial appearance and severe psychomotor retardation [Pitt et al., 1984]. Facial anomalies included prominent eyes, telecanthus, beaked nose with short upper lip, wide mouth and maxillary hypoplasia. They presumed that this combination was a new autosomal recessive syndrome. Donnai [1986] and Oorthuys and Bleeker-Wagemakers [1989] described another two patients. Recently Lindeman-Kusse et al. reported 2 patients in which a clinical diagnosis of Pitt-Rogers-Danks syndrome was made [Lindeman-Kusse et al., 1996]. At repeated examination, a deletion of the short arm of chromosome 4 was found in both. Originally a third patient was considered to possibly belong to the same group. However, this patient did not have a 4p deletion, but a different chromosome anomaly, as reported here.

The proposita was born in 1943. She was the oldest of 6 sibs. Her parents and sibs were normal. The parents were not consanguineous. No data about pregnancy and delivery of the patient are available. In the first year she had severe feeding problems. Developmental delay was evident from the beginning and at the age of 5 years she was admitted to an institution for the mentally handicapped.

At the age of 50 years she was evaluated for further diagnosis. Clinical examination showed a severely retarded woman without speech development. Height was 150 cm (<3rd centile); however measurement was unreliable due to her severe kyphoscoliosis. The cervical vertebral column was flexed to 90 degrees. She presented a thin habitus with underdeveloped muscles. Head circumference was 53 cm (3rd centile). Arms are kept flexed. She had a small, old looking face, prominent eyes, upward slant of palpebral fissures, hypertelorism (ICD=3.8 cm), slight ptosis, maxillary hypoplasia, and mandibular prognathism. Her nose was beaked with the tip overriding the upper lip. The philtrum was short and flat and covered by the columella of the nose. The lower lip was everted. She had a wide mouth. Both ears were large and protruding (Fig. 1). According to her family these facial characteristics have become more marked with age especially after puberty. Hands were relatively large, measuring 16 cm on both sides, and fleshy with deep palmar furrows; fingers were hyperextensible. She also had a flat umbilicus, bilateral drop-feet, and severe edema of the lower legs. Inspection of the external genitalia showed no anomalies. She has a shuffling gait and neurologic examination showed generalized hypertonicity. X-ray examination of the cervical vertebral column showed spina bifida occulta at C7. A clinical diagnosis of Pitt-Rogers-Danks syndrome was made. Analysis of GTG-banded chromosomes showed an aberrant chromosome 11 in all metaphases (Fig. 2). Chromosome painting demonstrated that the extra material was derived from chromosome 11. Subsequent FISH with probe cCL11-314, mapped to region 11q23.3-q24.1, showed one pair of fluorescent spots distal on both the normal and the derivative chromosome 11 (Fig. 3). Combining the results of FISH and chromosome banding we conclude that the karyotype is: 46,XX, dir dup(11)(pter→q23::q22→qter).

Fig.1 The proposita: Note prominent eyes, hypertelorism, tip of the nose overriding the upper lip and the everted lower lip.

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This report shows again that in case of a clinical diagnosis of Pitt-Rogers-Danks syndrome a chromosome anomaly may be the underlying defect. Furthermore it shows that the clinical picture of older patients with chromosome anomalies can be very different from that at young age and can mimic clinically recognizable syndromes of various causes.

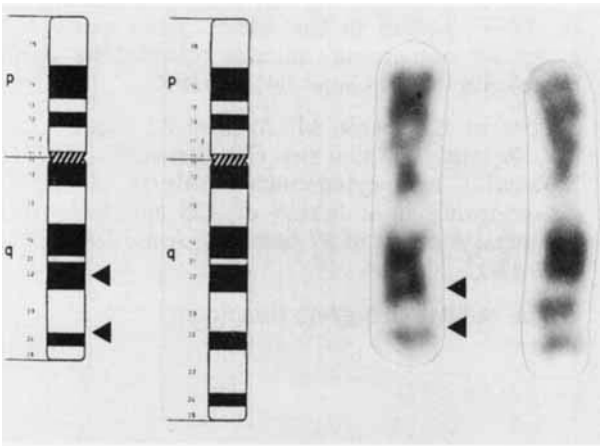

Figure 2: Partial karyogram showing G-banded normal chromosome 11 (left), derivative chromosome 11 (pter→q23::q22→qter) (right) and their idiograms. Arrows indicate the breakpoints, the region between the arrows is duplicated.

Figure 3: FISH with a centromere probe and probe cCL11-314, mapped to the region 11q23.3-q24.1 to a metaphase of the patient. Small arrows point to the centromeres, large arrows point to the signal distal on the q-arm of the normal chromosome 11 (left) and the derivative chromosome 11 (right).

REFERENCES

Donnai D (1986): A further patient with the Pitt-Rogers-Danks syndrome of mental retardation, unusual face, and intrauterine growth retardation. Am J Med Genet 24:29-32.

Lindeman-Kusse MC, van Haeringen A, Horweg-Nijman JJG, Brunner HG (1996): Cytogenetic abnormalities in two new patients with Pitt-Rogers-Danks phenotype. Am J Med Genet, this issue.

Oorthuys JWE, Bleeker-Wagemakers EM (1989): A girl with the Pitt-Rogers-Danks syndrome. Am J Med Genet
32: 140-141.

Pitt DB, Rogers JG, Danks DM (1984): Mental retardation, unusual face, and intauterine growth retardation: A new recessive syndrome? Am J Med Genet 19:307-313.

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